



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,968	05/10/2001	Eugene Y. Chan	C0989/7016(HCL)	5672

7590 10/28/2010
Helen C. Lockhart
c/o Wolf, Greenfield & Sacks, P.C.,
Federal Reserve Plaza
600 Atlantic Avenue
Boston, MA 02210-2211

EXAMINER

MUMMERT, STEPHANIE KANE

ART UNIT	PAPER NUMBER
----------	--------------

1637

MAIL DATE	DELIVERY MODE
-----------	---------------

10/28/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/852,968	Applicant(s) CHAN, EUGENE Y.	
	Examiner STEPHANIE K. MUMMERT	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 July 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 178-183 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 178-183 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>10/19/10</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment filed on July 21, 2010 is acknowledged and has been entered. Claims 178 and 179 are amended. Claims 1-177 have been canceled. Claims 182-183 have been added. Claims 178-183 are pending.

Claims 178-183 are discussed in this Office action.

All of the remaining amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL as necessitated by Amendment.

Previous Grounds of Rejection

The rejection of claims as lacking enablement is withdrawn in view of Applicant's amendment.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-

Art Unit: 1637

filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/037921 filed February 12, 1997, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The newly added claims specifically recite “emits the fluorescence signal in the absence of fluorescence resonance energy transfer”. However, the prior filed application is directed entirely to detection using RET or FRET detection. A careful review of the disclosure did not indicate the embodiment(s) claimed herein, where the marker is exposed to electromagnetic radiation and the signal is detected. Therefore, the claims will be afforded the filing date of the priority document with proper support for the claims, 60/064687, filed November 5, 1997.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 178-182 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yin et al. (Science, 1995, 270, 1653-1657) in view of Nie et al. (1995, Anal. Chem., 67(17), p. 2849-2857).

Art Unit: 1637

With regard to claim 178, Yin teaches a method comprising:
providing a nucleic acid, and detecting, while the nucleic acid is moved relative to
electromagnetic radiation by a tethered polymerase (Figure 1, where an RNA polymerase is
attached or tethered to a cover slip of a flow cell and the transcription process is monitored by
laser illumination or electromagnetic radiation).

With regard to claim 179, Yin teaches a method comprising:
moving a nucleic acid past electromagnetic radiation using a tethered polymerase,
exposing the nucleic acid to electromagnetic radiation, and detecting the nucleic acid (Figure 1,
where an RNA polymerase is attached or tethered to a cover slip of a flow cell and the
transcription process is monitored by laser illumination or electromagnetic radiation).

Regarding claim 178-182, Yin does not teach labeling with a unit specific marker.

Nie teaches real time detection of single molecules using confocal fluorescence
microscopy (Abstract).

With regard to claim 178, Nie teaches nucleic acid labeled with a unit specific marker
and detecting at least one FRET-independent fluorescent signal emitted from the unit (p. 2651,
col. 1, where DNA was labeled with a fluorescent dye, Figure 8).

With regard to claim 179, Nie teaches method for detecting a unit specific marker bound
to a nucleic acid comprising exposing a fluorescently labeled unit specific marker bound to the
nucleic acid and detecting an electromagnetic radiation signal from the fluorescently labeled unit
specific marker in the absence of fluorescence resonance energy transfer (p. 2651, col. 1, where
DNA was labeled with a fluorescent dye, Figure 8).

With regard to claim 182, Nie teaches an embodiment of claim 178, further including storing a signature of signals (p. 2651, col. 1, where DNA was labeled with a fluorescent dye, Figure 8, for example, where signals were stored over time).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Yin to include the fluorescent labeling of Nie to arrive at the claimed invention with a reasonable expectation for success. As taught by Nie, “through fluorescent labeling, single-molecule detection has been achieved for deoxynucleotides, oligonucleotides and double-stranded DNA molecules. The extraordinary sensitivity allows structural dynamics studies of individual DNA molecules labeled with only a few or a single fluorescent tag” (p. 2857, col. 1). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have adjusted the teachings of Yin to include the fluorescent labeling of Nie to arrive at the claimed invention with a reasonable expectation for success.

Claims 180-181 and 183 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yin et al. (Science, 1995, 270, 1653-1657) in view of Nie et al. (1995, Anal. Chem., 67(17), p. 2849-2857) as applied to claims 178-179 and 182, and further in view of Vurek et al. (US Patent 5,119,463; June 1992).

Regarding claims 180, while Yin and Nie teach apparatuses comprising a laser for detection, Yin and Nie are not specific regarding the presence of a waveguide. Vurek teaches the use of a waveguide in the detection (Abstract).

With regard to claim 180-181 and 183, Vurek teaches an embodiment of claim 178, wherein the electromagnetic radiation is transported through a waveguide (Abstract, Figure 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated a waveguide of the type described by Vurek into the method of fluorescence detection of Yin and Nie to arrive at the claimed invention with a reasonable expectation for success. As taught by Vurek, “The optical waveguide carries light signals at different wavelengths for monitoring oxygen concentration, carbon dioxide concentration, and pH levels. The probe is designed so that light signals used to monitor carbon dioxide concentration are optically prevented from impinging on the sensor used to monitor (Abstract)”. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have incorporated a waveguide of the type described by Vurek into the method of fluorescence detection of Yin and Nie to arrive at the claimed invention with a reasonable expectation for success.

Response to Arguments

Applicant's arguments with respect to claims 178-183 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

All claims stand rejected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Stephanie K. Mummert/
Primary Examiner, Art Unit 1637

SKM